



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

**OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD**

April 18, 2014

MEMORANDUM

SUBJECT: Formation of the Chemical Assessment Advisory Committee (CAAC) Augmented for the Review of the Draft IRIS Trimethylbenzenes Assessment

FROM: Thomas Carpenter
Designated Federal Officer (DFO)
EPA Science Advisory Board Staff Office (1400R)

THRU: Wanda Bright Ethics Officer /signed/
EPA Science Advisory Board Staff Office (1400R)

TO: Christopher S. Zarba
Director and Deputy Ethics Official
EPA Science Advisory Board Staff Office (1400R)

On January 17, 2014 the Science Advisory Board (SAB) Staff Office Director signed a memorandum that announced to the public the members of the SAB's Chemical Assessment Advisory Committee (CAAC) Augmented for the Review of the IRIS Toxicological Trimethylbenzenes Assessment. The memorandum provided a set of determinations that were necessary for forming the SAB Panel, and described all relevant information considered in forming the Panel, including a review of the confidential financial disclosure forms and evaluation of an appearance of a lack of impartiality. Since January 17, 2014, the SAB Staff Office rescheduled the Trimethylbenzene Review and meetings. Based on the set of determinations used in forming the CAAC Trimethylbenzene Review Panel and member's availability to participate in the rescheduled review, the members of the CAAC Trimethylbenzene Review Panel are as follows:

CAAC Trimethylbenzene Review Panel Members

Dr. Cynthia M Harris, Chair, Florida A&M University
Dr. Frederick Beland, National Center for Toxicological Research, U.S. Food and Drug Administration
Dr. James V. Bruckner, University of Georgia

Dr. Deborah Cory-Slechta, University of Rochester
Dr. Mitchell Cohen, New York University
Dr. Gary Ginsberg, Connecticut Department of Public Health
Dr. Helen Goeden, Minnesota Department of Health
Dr. Sean Hays, Summit Toxicology
Dr. Robert A. Howd, Tox Services
Dr. James E. Klaunig, Indiana University
Dr. Khannan Krishnan, Universite de Montreal
Dr. Lawrence Lash, Wayne State University
Dr. Frederick J Miller, Independent Consultant
Dr. Lorenz Rhomberg, Gradient, Inc
Dr. Stephen M. Roberts, University of Florida
Dr. Emanuela Taioli, State University of New York (SUNY) Downstate Medical Center
Dr. Raymond York, R.G.York & Associates

Concurred,

_____/signed/_____
Christopher S. Zarba
Director and Deputy Ethics Official
EPA Science Advisory Board Staff Office (1400R)

4/22/14
Date



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON D.C. 20460

**OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD**

January 17, 2014

MEMORANDUM

SUBJECT: Formation of the Chemical Assessment Advisory Committee (CAAC) Augmented for the Review of the Draft IRIS Trimethylbenzenes Assessment

FROM: Thomas Carpenter
Designated Federal Officer (DFO)
EPA Science Advisory Board Staff Office (1400R)

THRU: Wanda Bright /s/
Ethics Officer
EPA Science Advisory Board Staff Office (1400R)

TO: Christopher S. Zarba
Director and Deputy Ethics Official
EPA Science Advisory Board Staff Office (1400R)

The U.S. Environmental Protection Agency (EPA) requested the Science Advisory Board (SAB) to conduct a peer review its draft *IRIS Toxicological Review of Trimethylbenzenes* (August 2013). This toxicological review evaluated experimental animal data and other relevant noncancer data. The assessment includes an inhalation reference concentration, an oral reference dose, and a qualitative cancer descriptor for each trimethylbenzene isomer. The assessment does not include a quantitative cancer assessment.

This memorandum addresses the set of determinations that were used in forming the CAAC Trimethylbenzene Review Panel including:

1. The type of review body that will be used to conduct the review, and the nature of the review;
2. The types of expertise needed to address the general charge;

3. Financial conflict of interest considerations, including identification of parties who are potentially interested in or may be affected by the topic to be reviewed;
4. How regulations concerning “appearance of a loss of impartiality” pursuant to 5 C.F.R. § 2635.502 apply to members of the Panel;
5. Other considerations that might affect the objectivity of members of the Panel; and
6. How individuals were selected for the Panel.

DETERMINATIONS:

1. The type of review body that will be used to conduct the review and the nature of this review.

The Chemical Assessment Advisory Committee (CAAC), a standing committee of the SAB, will be augmented by subject matter experts to form a panel to conduct a peer review of the draft *IRIS Toxicological Review of Trimethylbenzenes* (August 2013). The CAAC Trimethylbenzene Review Panel will provide independent advice through the chartered SAB on the EPA’s scientific and technical assessments that support the agency’s toxicological review of trimethylbenzenes. The assessment is the first IRIS assessment developed for trimethylbenzenes and includes the Reference Dose and Reference Concentration for the three trimethylbenzene isomers, 1,2,3-TMB; 1,2,4-TMB; 1,3,5-TMB.

The types of expertise needed to address the general charge.

EPA Charge questions seek the SAB’s advice and comment of the scientific and technical literature used to support the assessment, the synthesis of evidence for hazard identification, and the toxicokinetic analysis to support the development of reference concentration and reference dose in the draft *IRIS Toxicological Review of Trimethylbenzenes*. The charge questions also seek feedback on whether the document is clear and concise, a central concern expressed in the NRC report *Review of the Environmental Protection Agency’s Draft IRIS Assessment of Formaldehyde* (NRC 2011).

On August 28, 2013, the EPA SAB Staff Office announced in a Federal Register Notice (Volume 78, Number 167, Pages 53144-46) that it was forming a panel to review and provide independent expert advice through the Chartered SAB on the EPA’s draft *Toxicological Review of Trimethylbenzenes*. The SAB sought public nominations of nationally recognized and qualified experts in one or more of the following areas, particularly with respect to trimethylbenzenes: developmental neurotoxicity, developmental toxicity, physiologically-based pharmacokinetic (PBPK) modeling, respiratory and inhalation toxicology, hematological toxicology, and carcinogenicity.

2. Financial conflict of interest consideration, including identification of parties who are potentially interested in or may be affected by the topic reviewed.
 - (a) Identification of parties (or class of parties) whose financial interests may be affected by the matter to be reviewed: The principal interested and affected parties as a class for this topic are: organizations involved in processes that could be considered part of the life-cycle of the chemical (i.e., trimethylbenzene) to be considered by the Panel (including, but not limited to, manufacture, use, distribution, treatment and disposal).

(b) Conflict of interest considerations: For Financial Conflict of Interest (COI) issues, the basic 18 U.S.C. § 208 provision states that: “An employee is prohibited from participating *personally or substantially* in an official capacity in any *particular matter* in which he, to his knowledge, or any person whose interests are imputed to him under this statute has a *financial interest*, if the particular matter will have a *direct and predictable effect* on that interest [emphasis added].” For a conflict of interest to be present, all elements in the above provision must be present. If an element is missing the issue does not involve a financial conflict of interest; however, the general provisions in the appearance of impartiality guidelines still apply and need to be considered.

(i) Does the general charge to the CAAC trimethylbenzene Review Panel involve a particular matter? A “particular matter” refers to matters that “...will involve deliberation, decision, or action that is focused upon the interest of specific people, or a discrete and identifiable class of people.” It does not refer to “...consideration or adoption of broad policy options directed to the interests of a large and diverse group of people.” [5 C.F.R. § 2640.103(a)(1)]. A particular matter of general applicability means a particular matter that is focused on the interests of a discrete and identifiable class of persons, but does not involve specific parties [5 C.F.R. § 2640.102(m)].

The activity of this augmented CAAC Panel will qualify as a *particular matter of general applicability* because the resulting advice will be part of a deliberation, and under certain circumstances the advice could involve the interests of a discrete and identifiable class of people but does not involve specific parties. That group of people constitutes those who are involved with organizations facing regulatory decisions informed by the IRIS Trimethylbenzene health assessment that may impact the manufacture, distribution, treatment or disposal of trimethylbenzenes.

(ii) Will there be personal and substantial participation on the part of the panel members? Participating personally means direct participation in this review. Participating substantially refers to involvement that is of significance to the matter under consideration.[5 C.F.R. §2640.103(a)(2)]. For this review, the SAB Staff Office has determined that the *CAAC Trimethylbenzene Review Panel members will be participating personally in the matter*. Panel members will be providing the agency with advice and recommendations on the agency’s trimethylbenzene toxicological analyses, and such advice is expected to directly influence the agency’s risk assessment and risk management decisions involving trimethylbenzenes. *Therefore, participation in this review also will be substantial.*

(iii) Will there be a direct and predictable effect on panel members’ financial interests? A direct effect on a participant’s financial interest exists if “... a close causal link exists between any decision or action to be taken in the matter on the financial interest..... A particular matter does not have a direct effect ... if the chain of causation is attenuated or is contingent upon the occurrence of events that are speculative or that are independent of, and unrelated to, the matter. A particular matter that has an effect on a financial interest only as a consequence of its effects on the general economy is not considered to have a direct effect.” [5 C.F.R. § 2640.103(a)(ii)]. CAAC members and prospective panelists were asked to submit EPA Form 3110-48, a Confidential Financial Disclosure for Special Government Employees, so that the SAB Staff Office could make this determination. *The*

SAB Staff Office has determined that there will be no direct and predictable effect on the financial interests of CAAC Trimethylbenzene Review Panel members from their participation on the panel.

3. How regulations concerning “appearance of a loss of impartiality” pursuant to 5 C.F.R. § 2635.502 apply to members of the Panel.

The Code of Federal Regulations at 5 C.F.R. § 2635.502(a) states that: “Where an employee knows that a *particular matter involving specific parties* is likely to have a direct and predictable effect on the financial interest of a member of his household, or knows that a person with whom he has a covered relationship is or represents a party to such matter, and where the person determines that the circumstances would cause a reasonable person with knowledge of the relevant facts to question his impartiality in the matter, the employee should not participate in the matter unless he has informed the agency designee of the appearance problem and has received authorization from the agency designee.”

Further, § 2635.502(a)(2) states that, “An employee who is concerned that circumstances other than those specifically described in this section would raise a question regarding his impartiality should use the process described in this section to determine whether he should or should not participate in a particular matter.”

Prospective panel members were evaluated against the 5 C.F.R. 2635(a)(2) general requirements for considering an appearance of a loss of impartiality. This evaluation included information provided on the EPA Form 3110-48 confidential financial disclosure forms. *The SAB Staff Office has determined that the matter to be considered by the CAAC Trimethylbenzene Review Panel is not a particular matter involving specific parties; i.e., this matter does not involve “any judicial or other proceeding, application, request for a ruling or other determination, contract, claim, controversy, investigation, charge, accusation, arrest or other particular matter involving a specific party or parties in which the United States is a party or has a direct and substantial interest” [5 C.F.R. 2637.102(a)(7)].*

4. Other considerations that might affect the objectivity of members of the Panel.

Members of SAB panels must be scientific and technical experts who are objective and open-minded, able to engage in deliberative discussions with scientists who may have disparate perspectives. To evaluate candidates, the SAB Staff Office considers information provided by the public in response to the invitation for public comment on the candidates, information provided by candidates (including on the EPA Form 3110-48), and information independently gathered by SAB staff.

As part of a determination that panel members are objective and open-minded on the topic of the review, and consistent with the agency’s Peer Review Policy, the SAB Staff Office considers previous involvement in the matter before the Panel. This evaluation includes responses provided by candidates to the following questions:

- (a) Do you know of any reason that you might be unable to provide impartial advice on the matter to come before the panel/committee/subcommittee or any reason that your impartiality in the matter might be questioned?

- (b) Have you had any current or previous involvement with the review document(s) under consideration including authorship, collaboration with the authors, or previous peer review functions? If so, please identify and describe that involvement.
- (c) Have you served on previous advisory panels, committees or subcommittees that have addressed the topic under consideration? If so, please identify those activities.
- (d) Have you made any public statements (written or oral) on the issue that would indicate to an observer that you have taken a position on the issue under consideration? If so, please identify those statements.

The SAB Staff Office has determined that there is no reason to believe that the members selected for the CAAC Trimethylbenzene Review Panel would not be objective and open-minded and able to engage in deliberative discussions with scientists who may have disparate points of view on the matter before the Panel.

5. How individuals were selected for the Panel.

On December 11, 2013, the SAB Staff Office posted a list of 38 candidates for the Panel, identified based on their expertise and willingness to be considered for the panel. This list was accompanied by a notice inviting public comments on the list of candidates, to be submitted by January 6, 2014. The SAB Staff Office received one comment on a candidate for the Panel from Dr. Richard Dennison on behalf of the Environmental Defense Fund.

The SAB Staff Office Director makes the final decision about who serves on the Panel based on all of the relevant information, including a review of each candidate's confidential financial disclosure form (EPA Form 3110-48), the responses to the questions above, public comments, and information independently gathered by SAB Staff.

For the SAB Staff Office, a balanced committee or panel is characterized by candidates who possess the necessary domains of scientific knowledge, relevant perspectives (which, among other factors, can be influenced by work history and affiliation), and the collective breath of experience to adequately address the general charge. Specific criteria to be used in evaluating an individual panel member include: (a) scientific and/or technical expertise, knowledge, and experience; (b) availability and willingness to serve; (c) absence of financial conflicts of interest; (d) absence of an appearance of a loss of impartiality pursuant to 5 C.F.R. § 2635.502; (e) skills working on advisory committees and panels (including objectivity and open-mindedness); and (f) for the committee as a whole, diversity of scientific expertise and viewpoints.

On the basis of the above-specified criteria, the members of the CAAC Trimethylbenzene Review Panel are as follows:

CAAC Trimethylbenzene Review Panel Members

Dr. Cynthia M Harris, Chair, Florida A&M University
Dr. Frederick Beland, National Center for Toxicological Research, U.S. Food and Drug Administration
Dr. James V. Bruckner, University of Georgia
Dr. Deborah Cory-Slechta, University of Rochester
Dr. William Michael Foster, Duke University Medical Center
Dr. Gary Ginsberg, Connecticut Department of Public Health
Dr. Helen Goeden, Minnesota Department of Health
Dr. Sean Hays, Summit Toxicology
Dr. Robert A. Howd, Tox Services
Dr. James E. Klaunig, Indiana University
Dr. Khannan Krishnan, Universite de Montreal
Dr. Lawrence Lash, Wayne State University
Dr. Frederick J Miller, Independent Consultant
Dr. Lorenz Rhomberg, Gradient, Inc
Dr. Stephen M. Roberts, University of Florida
Dr. Emanuela Taioli, State University of New York (SUNY) Downstate Medical Center
Dr. Raymond York, R.G.York & Associates

Concurred,

_____/signed/
Christopher S. Zarba
Director and Deputy Ethics Official
EPA Science Advisory Board Staff Office (1400R)

January, 17, 2014
Date